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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/066,551	01/31/2002	Michael A. Apicella	875.045US1	2735

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SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. BOX 2938
MINNEAPOLIS, MN 55402

EXAMINER	
BASKAR, PADMAVATHI	

ART UNIT	PAPER NUMBER
1645	9

DATE MAILED: 07/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application No.	Applicant(s)	
	10/066,551	APICELLA ET AL.	
	Examiner	Art Unit	
	Padmavathi v Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sh et with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-58* is/are pending in the application.

4a) Of the above claim(s) *2-4, 6, 8-14 , 16-18, 20, 22 ,26- 58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 5, 7,15, 19, 21 and 23-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-58* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5/7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The response filed 4/30/03 Paper # 8 has been entered into the record. Claims 1-58 are pending in the application.

Drawings

2. The drawings are objected for the reasons set forth on the enclosed PTO-948. A proposed drawing correction or corrected drawings are required in reply to this Office action to avoid abandonment of the application.

Information Disclosure Statement

3. The information disclosure statements 8/5/02 (paper # 5) and 3/10/03 (Paper # 5) have been considered and an initialed copy is enclosed.

Election/Restriction

4. Applicant's election with traverse of Group II, Claims 1-7, 15-25 and 57, SEQ ID N0: 4 in Paper # 8, 4/30/03 is acknowledged. The examiner regrets the oversight made in the restriction in paper # 6 in including the claim 57 to Group II. Claim 57 is directed to a DNA vaccine and should have been in Group I. Therefore, claim 57 is included in group I, drawn to DNA. The traversal is on the ground(s) that all SEQ.ID.NO: 1-12 should be examined as the claims recite Markush group of sequences and the search and examination of the other sequences would not be an undue burden. This is not found persuasive.

MPEP 803 states that restriction is proper between patentably distinct inventions where the inventions are (1) independent or distinct as claimed and (2) a serious search and examination burden is placed on the examiner if restriction is not required. It is noted that the restriction of one SEQ.ID.NO is not an election of species. The examiner made it clear on the record in paper # 6 (3/25/03) (paragraph # 3) that the disclosed sequences are considered as patentably distinct and different inventions since each SEQ.ID.NO is distinct in containing

different amino acids and given a specific sequence identification number. Restrictions between the inventions, SEQ.ID.NO: 1-12 is deemed to be proper for the reasons previously set forth. In regard to burden of search and examination, MPEP 803 states that a burden can be shown if the examiner shows either separate classification, different field of search or separate status in the art. In the instant case, the restriction of sequences has acquired a separate status in the art as a separate subject for inventive effect and requires independent searches. The search for each of the above inventions is not co-extensive particularly with regard to the literature search. A reference, which would anticipate the invention of one SEQ.ID.NO, would not necessarily anticipate or make obvious any of the other SEQ.ID.NO. Moreover, as to the question of burden of search, classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Burden in examining materially different groups having materially different issues also exist.

Each of the recited sequences was deemed patentably distinct from each other and applicants were required to elect a single product for examination on the merits as set forth in paper # 6. Applicants indicate that with respect to the species election, they elect SEQ ID NO: 4. As such, examination of the single product will be restricted to SEQ ID NO: 4. Restriction is deemed proper because these products appear to constitute patentably distinct inventions and is therefore made FINAL.

5. Claims 8-14 and 26-58 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected group of inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 8.

6. Claims 2-4,6,16-18, 20, 22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non elected inventions of SEQ.ID.NOS there being no

allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 8.

7. Claims 1, 5, 7,15, 19, 21 and 23-25 will only be examined to the extent they read on the elected invention of SEQ ID N0: 4, all other sequence identifiers are withdrawn from consideration based on non-elected inventions as set forth in the restriction requirement.

8. Applicant is advised to restrict claims 1 and 15 to elected invention to recite p55 (SEQ.ID.NO: 4), the elected invention.

Priority

9. This application claims domestic priority under 35, U.S.C. 119 (e) to provisional applications

60/266070	1/31/01
60/310356	8/6/01
60/344452	10/23/01

The examiner has reviewed the applications and priority is accorded as of 1/31/01 to claims 1, 5, 7,15, 19, 23-25 with respect to polypeptide SEQ ID N0: 4 as the provisional application disclosed said SEQ.ID.NO: 4 containing 525 amino acids.

Claim rejections 101

10. 35 U.S.C. 101 reads as Follows
> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

11. Claim 1 is rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter. The product, polypeptide as claimed, has the same characteristics as that found in nature. To overcome this rejection the Examiner suggests the amendment of the claims to include purity limitations, which would distinguish the characteristics of applicant's

product from the product, as it exists in nature. It is further suggested that such limitation include the terminology " purified and isolated" (i.e. if such purity is supported in the specification) and/or a description of what applicant's protein is "free of" relative to the natural source. (see Farbenfabriken of Elberfeld Co. v. Kuehmsted, 171 Fed. 887, 890 (N.D. Ill. 1909) (text of claim at 889); Parke-Davis & Co. v. H.D. Mulford Co., 189 Fed. 95, 103, 106, 965 (S.D.N.Y. 1911) (claim 1); and In re Bergstrom, 427 F.2d 1394, 1398, 1401-1402 (CCPA 1970).

Claim Rejections - 35 USC 112, first paragraph

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 15, 19 and 21 (vaccine composition) are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Instant claims are evaluated for enablement using the Wands analysis. Many of the factors regarding undue experimentation have been summarized in In re Wands, 858 F.2d 731,8 USPQ2d 1400 (Fed.Circ.1988) as follows:

(1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence

of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

Enablement of a "vaccine composition" is considered to rest on a teaching of in vivo administration for purposes consistent with the intended use disclosed in the specification. The disclosed intended use for the claimed vaccine is for the treatment of sexually transmitted gonorrhea disease caused by *Neisseria gonorrhea* infections. Thus, the nature of the invention is a therapeutic vaccine composition used in treatment or prevention. In addition, the instant specification does not teach how to use the vaccine comprising an immunogenic amount of polypeptide SEQ.ID.NO: 4, without undue experimentation, for the prevention, treatment, or cure of a disease in the female patients to which the substance is administered.

The specification discloses the claimed composition can be used as a vaccine. There is insufficient guidance, which would enable one, skilled in the art to use the claimed compositions for their intended purpose, viz., for the generation of a protective immune response against gonorrhea disease caused by Neisseria gonorrhea. At the time the invention was made, vaccines comprising the claimed polypeptide were not routinely used for the treatment of gonorrhea disease caused by Neisseria gonorrhea. The specification lacks guidance by way of general methods or working examples which teach an "effective amount" of the vaccine which would be used for this purpose. Lack of working examples is given added weight in cases involving an unpredictable and undeveloped art, such as immunotherapy gonorrhea disease caused by Neisseria gonorrhea. It is unpredictable whether the claimed composition, which is disclosed as being only immunogenic, would have the added property of generating the protective immune response sufficient to inhibit gonorrhea disease caused by Neisseria gonorrhea because the prior art discloses that the human pathogen *N.gonorrhoeae* is endowed with a wide range of mechanisms that facilitate immune avoidance including antigenic shift in

the expression of surface antigens. Because of this antigenic shift the development an effective vaccine has resulted in frustrated attempts (see introduction of Paz et al 1995, Microbiology 141, 913-920). Therefore, it is important to study how this bacterium invades the epithelial cells, the expression of intercellular adhesion molecules on epithelial cells and the surface antigens of bacteria during the process of invasion first. Applicant's specification (page 2) states that mechanisms by which the gonococcus infects and invades the female genital tract are only at the beginning stage. The specification has not disclosed a link or nexus between the generation of protective immunity and the claimed polypeptide. Further, it is not routine in the art of immunotherapy to use the claimed compositions for this purpose. Accordingly, there is no objective basis upon which the skilled artisan would reasonably be able to determine or predict an amount of the claimed composition/vaccine effective for its intended use. Therefore, undue experimentation would be required to make and use the invention.

Claim Rejections - 35 USC 112, second paragraph

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

15. Claims 1, 5 and 7are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 5 are rejected as being vague and indefinite for the recitation of "A polypeptide comprising a polypeptide p55 " Does applicant intend to mean an isolated protein comprising the 55 KD polypeptide (p55) from *N.gonorrhoeae?*

Claim 7 recites the limitation "protein" in line 1. There is insufficient antecedent basis for

this limitation in the claim.

Claim R j ctions - 35 USC 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

17. Claims 1,5,7 and 15, 19, 21 and 23-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Paz et al 1995, Microbiology 141, 913-920.

Claims are directed to an isolated protein comprising polypeptide p55 and said polypeptide has an amino acid sequence matching the amino acid sequence of SEQ.ID.NO: 4. Claims are also drawn to a vaccine composition comprising an immunogenic amount of polypeptide p55 and adjuvant, said polypeptide is encoded by nucleic acid, said polypeptide linked to second polypeptide or polysaccharide.

Examiner is viewing the vaccine as a composition

Paz et al disclose outermembrane proteins from *N.gonorrhoeae* strain p9. (see page 914, right column under Methods, first paragraph). Outer membrane proteins (OMP) from *N.gonorrhoeae would* inherently contain the claimed protein and several other proteins that are linked together Monoclonal antibodies were directed against polysaccharides and outermembrane proteins (see page 914, right column under Methods, second paragraph) indicating that the composition is immunogenic. It is routine in the art to use adjuvants such as CFA for immunizing mice for raising antibodies. Applicant's use of the open-ended term "comprising " in the claims 1 and 15

fails to exclude unrecited steps or ingredients and leaves the claims open for inclusion of unspecified ingredients, even in major amounts. Therefore, the claims read on the disclosed OMP from *N.gonorrhoeae*. Characteristics such as amino acid sequence as set forth in the SEQ.ID.NO: 4 are considered inherent properties of the outer membrane proteins and proteins are encoded by nucleic acids. See In re Horvitz, 168 F 2d 522, 78 U.S.P.Q. 79 (C.C.P.A. 1948) and Ex parte Davis et al., 80 U.S.P.Q. 448 (PTO d. App. 1948). In the absence of evidence to the contrary the disclosed prior art anticipates the claimed invention. Since the Office does not have the facilities for examining and comparing applicants' claimed isolated polypeptide p55 comprising SEQ.ID.NO: 4 with the outer membrane protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. Here, the prior art discloses the same composition and formulations thereof as claimed. Thus, the prior art anticipated the claimed invention.

It is acknowledged that weight is given to every term in claims 15, 19, 21 and 23-25. This is why the instant claims drawn to vaccine is scrutinized differently from a composition claim under 112, first paragraph. However, under prior art rejections, the term vaccine must be weighed with the structural limitations of the claim. If the immunogenic composition i.e., vaccine merely comprises a known composition, the term carries little weight absent evidence of structural difference. However, under prior art rejections, the term vaccine is considered as a composition comprising an isolated polypeptide. See In re Best, 562 F. 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

18. Claims 1, 5, 7, 15, 19 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Fraser et al 1999, Accession Number AAY 75751.

The claims are discussed supra.

Fraser et al disclose a novel polypeptide from *N.gonorrhoeae*. (See the attached sequence alignment and abstract) comprising an amino acid sequence, which is 98.2% similar to the claimed SEQ.ID.NO: 4. The polypeptide could be used as vaccine, immunogenic composition or to raise antibodies (see abstract) The antigen to which an immune response has to be elicited is in general in hydrophilic phase, buffer or saline and is routinely used in the art. Characteristic such as p55 is considered as the inherent property of the disclosed polypeptide that is encoded by nucleic acid. In the absence of evidence to the contrary the disclosed prior art anticipated the claimed invention.

It is acknowledged that weight is given to every term in claims 15, 19 and 21 This is why the instant claims drawn to vaccine is scrutinized differently from a composition claim under 112, first paragraph. However, under prior art rejections, the term vaccine must be weighed with the structural limitations of the claim. If the immunogenic composition i.e., vaccine merely comprises a known composition, the term carries little weight absent evidence of structural difference. However, under prior art rejections, the term vaccine is considered as a composition comprising an isolated polypeptide. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

19. Claims 1, 5, 7, 15, 19 and 21 are rejected under 35 U.S.C. 102(a) as being anticipated by Parkhill 2000, Accession Number B81859.

The claims are discussed supra.

Parkhill et al disclose a novel polypeptide from *N.meningitidis.* (see the attached sequence alignment and abstract) comprising an amino acid sequence, which is 100% similar to the claimed SEQ.ID.NO: 4. Characteristic such as p55 is considered as the inherent property of the disclosed polypeptide that is encoded by nucleic acid. Since this polypeptide is 100%identical to the claimed polypeptide the source from which it is isolated is considered as a

product by process claim. When the reference teaches a product that appears to be the same as, or an obvious variant of, the product set forth in a product-by-process claim although produced by a different source. See In re Marosi, 710 F.2d 799, 218 USPQ 289 (Fed. Cir. 1983) and In re Thorpe, 777 F.2d 695, 227 USPQ 964 (Fed. Cir. 1985). See also MPEP § 2113. Thus, the prior art anticipated the claimed invention.

It is acknowledged that weight is given to every term in claims 15, 19 and 21 This is why the instant claims drawn to vaccine is scrutinized differently from a composition claim under 112, first paragraph. However, under prior art rejections, the term vaccine must be weighed with the structural limitations of the claim. If the immunogenic composition i.e., vaccine merely comprises a known composition, the term carries little weight absent evidence of structural difference. However, under prior art rejections, the term vaccine is considered as a composition comprising an isolated polypeptide. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

20. Claims 1,5, 7, 15, 19 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Cann et al 1989, J.Med.Microbiology 30, 23-30.

The claims are discussed supra

Cann et al discolse an isolated antigen comprising a polypeptide p55kD from *N.meningitidis*. (see abstract, page 25, right column, first paragraph). Antigen was prepared from strains of *Neisseria* (see page 24, left column, last paragraph) in saline (pharmaceutical carrier). Characteristic such as amino acid sequence SEQ.ID.NO: 4. is an inherent property of p55 polypeptide and is known in the art that the polypeptide comprising SEQ.ID.NO: 4. from *N.meningitidis* is 100% identical with *N.gonorrhoeae* (as shown by Park et al). When the reference teaches a product that appears to be the same as, or an obvious variant of, the product set forth in a product-by-process claim although produced by a different source. See In

re Marosi, 710 F.2d 799, 218 USPQ 289 (Fed. Cir. 1983) and In re Thorpe, 777 F.2d 695, 227 USPQ 964 (Fed. Cir. 1985). See also MPEP § 2113. Thus, the prior art anticipated the claimed invention.

It is acknowledged that weight is given to every term in claims 15, 19 and 21. This is why the instant claims drawn to vaccine is scrutinized differently from a composition claim under 112, first paragraph. However, under prior art rejections, the term vaccine must be weighed with the structural limitations of the claim. If the immunogenic composition i.e., vaccine merely comprises a known composition, the term carries little weight absent evidence of structural difference. However, under prior art rejections, the term vaccine is considered as a composition comprising an isolated polypeptide. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594. Thus, the prior art anticipated the claimed invention.

Specification Informalities

21. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, see in particular at least page 22.
Applicant is required to delete the embedded hyperlink and/or other form of browser- executable code. See MPEP § 608.01.
Applicant is advised to remove " fill in once studies completed" on page 81.

Status of Claims

22. No claims are allowed.

23. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padma Baskar whose telephone number is (703) 308-8886. The examiner can normally be reached on Monday through Friday from 6:30 AM to 4 PM EST

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Padma Baskar Ph.D.

7/18/03

NITA MINKFIELD
PRIMARY EXAMINER